

### Amendments to the Specification:

Please replace the paragraph starting at page 1, line 11 with the following paragraph:

Adenovirus is a non-enveloped ~~double-stranded~~ double-stranded DNA virus, and causes insignificant upper respiratory tract infections, keratoconjunctivitis, enterogastritis, and the like in humans. The adenovirus genomes are approximately 36kb, and easy to handle by using conventional recombinant DNA technology. Cell endosmosis of virus is initialized by binding of a fiber knob protein of adenovirus to ~~Coxsackie~~ Coxsackie & Adenovirus receptor (CAR) on the cell surface. Subsequently, via the interactions between integrins ( $\alpha v\beta 3$ ,  $\alpha v\beta 5$ ) on the cell surface and the capsid penton base, the virion is introduced into the cell by the clathrin coated endocytosis. Then, the conformational changes of virion capsid proteins are derived, as the low pH condition of the endosome, allowing the release of the virion capsid proteins to the cytoplasm. Following the protein release, the capsid proteins translocate to the nucleus, where its replication and transcription ~~is-being~~ are carried out. Transcription of genes can be divided into two different types, for early genes (E) which are expressed before the replication, and late genes (L) which are expressed after the replication. Adenovirus used for gene therapy lacks the E1 gene area, resulting incomplete replication, thereby being used in a form containing other DNAs inserted thereto. Therefore, the recombinant adenovirus vectors can be cultured to increase in cell lines such as HEK293 which can express E1 genes continuously.

Please replace the paragraph starting at page 2, line 9 with the following paragraph:

Retrovirus with envelope is a single stranded RNA virus having a diploid genome of about 7~10kb, and comprises the four gene groups called *gag*, *pro*, *pol*, and *env*, respectively. Each of the gene group encodes the structural capsid protein, viral protease, integrase, reverse transcriptase, envelope and glycoprotein, etc. The retrovirus has a packing ~~signal( $\psi$ )~~ signal ( $\psi$ ) referred as ~~long-terminal-repeat(LTR)~~ long-terminal repeat (LTR), and a cis-acting sequence. Retrovirus infection of a cell can be achieved by primarily binding of the envelope glycoprotein to its cell surface receptor, and subsequent fusing of the virus envelope with the cell membrane, thereby internalizing the capsid nucleus into the cell. Once the capsid has entered into the cytoplasm, the reverse transcriptase inside the capsid produces double stranded proviral genome, which forms a complex with an integrase and moves to the nuclear membrane. When the nuclear membrane disappears during ~~[[the]]~~ mitosis, the complex ~~becomes-to-enter~~ enters into the nucleus. The proviral genome introduced into the nucleus inserts into a chromosome of the host by means of ~~[[the]]~~ an integrase to express the viral genome by using the transcription apparatus of the host. The recombinant retrovirus vector

~~does~~ does not express any viral gene that makes this distinguished from the above-mentioned adenovirus vectors, as all of its genes are replaced to marker or therapeutic genes except LTRs and  $\psi$  sequence. To cultivate such recombinant retrovirus, the viral genes of *gag*, *pol*, and *env* should be expressed in a trans form, which can be achieved by using cell lines that express these genes in a stable manner.

Please replace the paragraph starting at page 4, line 1 with the following paragraph:

Herpes simplex virus-1 is a double stranded DNA virus having an envelope. It encodes 80 or more genes from its 152kb genomes, and has a significantly wide range of ~~[[host]]~~ hosts as its envelope glycoproteins (gB, gC) ~~are binded~~ bind to the extracellular heparan sulphate that is discovered from the all kinds of cell membrane. When the virus is being entered into the host cell, the virus envelope glycoprotein gD and the fibroblast growth factor (FGF) receptor of the host are necessary. Herpes simplex virus vector can be divided into two types: a recombinant herpes simplex virus vector and an amplicon vector, wherein the recombinant herpes simplex virus vector has a transcription unit directly inserted in its genome, and the amplicon vector is a plasmid infected with a helper virus, wherein the said plasmid contains the transcription unit, replication origin, and packing signal. The amplicon vector is subjected to the rolling circle replication, producing a herpes simplex virus having an insertion of multiple copy genes during packing procedure.

Please replace the paragraph starting at page 4, line 15 with the following paragraph:

Those above-mentioned virus vectors have their own advantages and disadvantages. Common problems to these above virus vectors include the limitation of the cell ranges, which could be infected by them, i.e., the limitation in cells which could ~~recept~~ receive them, and the inactivation by immune responses of host. As these types of vectors have such limitations, they are not applicable to all kinds of cells.

Please replace the paragraph starting at page 5, line 11 with the following paragraph:

Still another object of the present invention is to provide a method of producing a peptide-DNA complex comprising covalently linking the peptide of ~~sequence-ID-No.-1~~ SEQ ID NO:1 and the DNA of ~~sequence-ID-No.-2~~ SEQ ID NO:2, and hybridizing the DNA of ~~sequence-ID-No.-3~~ SEQ ID NO:3 to the DNA of ~~sequence-ID-No.-2~~ SEQ ID NO:2.

Please replace the paragraph starting at page 6, line 5 with the following paragraph:

The peptide vector according to the present invention is composed of a leader peptide, a linker DNA, and a desired gene. The leader peptide (~~seq-ID-No.-1~~ SEQ ID NO:1) has a structure shown below; the amino acid sequence was deduced by analyzing proteins which are expected to have a fusion ability of cell membrane in various viruses having envelope, for

example, retrovirus, paramixovirus and the like. This sequence is introduced into a cell directly through the cell membrane.

Please replace the paragraph at page 6, line 11 with the following paragraph:

<Leader peptide: ~~seq. ID No. 1~~ SEQ ID NO:1>

Please replace the paragraph starting at page 6, line 17 with the following paragraph:

The linker DNA, composed of 15 to 18 bases, connects a leader peptide and a desired gene, and has a structure as below:

linker-1 (~~seq. ID No. 2~~ SEQ ID NO:2): 5'-Cys-CTA-ATA-CGA-CTC-ACT-AT-3'

linker-2 (~~seq. ID No. 3~~ SEQ ID NO:3): 3'-GA-TAT-GCT-GAG-TGA-T-5'

Please replace the paragraph starting at page 8, line 5 with the following paragraph:

Only one strand (linker-1, ~~seq. ID No. 2~~ SEQ ID NO:2) of complementary double strand of the linker DNA is covalently bonded with a leader peptide, thus when the linker is binding with the desired gene, only the other strand (linker-2, ~~seq. ID No. 3~~ SEQ ID NO:3) which is not covalently bonded with the leader peptide, can be covalently bonded with the desired gene, so it can be easily separated from the leader peptide under the inner environment of the nucleus. Thus, since both ends of separated genes are single-stranded, it is possible to be readily integrated into the inner part of the host chromosome later.

Please replace the paragraph at page 10, line 4 with the following paragraph:

Leader peptide (~~Seq. No. 1~~ SEQ ID NO:1) was synthesized by Fmoc-solid phase method.

Please replace the paragraph starting at page 10, line 5 with the following paragraph:

To linker-1 DNA (~~Seq. No. 2~~ SEQ ID NO:2), cystein was attached in order for binding with the leader peptide, and to the 5' end of linker-2 DNA (~~Seq. No. 3~~ SEQ ID NO:3), phosphate group was attached by T4 polykinase in order for binding with the marker gene.

Please replace the paragraph starting at page 11, line 15 with the following paragraph:

The expression of transgenes injected ~~[[to the]]~~ into each tissue was investigated by PCR after extracting mRNA from brain and muscle tissue, and synthesizing cDNA.

Please replace the paragraph starting at page 11, line 17 with the following paragraph:

The transgenes obtained from example 3 were intravenously injected to a male mouse (200g weight) with a dose of 500ng/day, at day 1, 3 and 5, then the mouse was euthanized at day 6. mRNA was extracted from brain and muscle tissue samples of the mouse, by using mRNA purification kit (~~ambion~~ Ambion™, Inc. (Austin, Texas), Cat. No. 1918).

Please replace the paragraph starting at page 12, line 1 with the following paragraph:

1  $\mu$ g of the extracted mRNA, 50 pmols of ~~oligo-dT~~ oligo-dT or random primer and ~~RNase inhibitor(40 units)~~ RNase inhibitor (40 units) were added thereto, and the total volume was adjusted to 50  $\mu$ l by adding distilled water, denatured at 96°C for 10 minutes, and annealed at 60°C for 30 minutes. Reaction buffer, 1.25mM of dNTP, 2mMs DTT, ~~RNase inhibitor(40 units)~~ RNase inhibitor (40 units), and MMLV reverse ~~transcriptase(200 units, ambion)~~ transcriptase (Ambion™, Inc. (Austin, Texas)) were added thereto, and reacted at 42°C for 1 hour. After completing the reaction, it was precipitated and purified by isopropanol and ethanol, and resuspended into distilled water.

Please replace the paragraph starting at page 12, line 9 with the following paragraph:

After synthesizing cDNA, PCR was performed using GFP specific primer[~~GFP-f(Seq. ID No. 4)~~ GFP-f (SEQ ID NO:4), ~~GFP-r (Seq. ID No. 5)~~ GFP-r (SEQ ID NO:5)] was performed by Taq polymerase (~~Takara TaKaRa™ Bio, Inc. (Japan)~~). After completing the PCR, electrophoresis was carried out on the 2% agarose gel to find a band.

<GFP specific primer>

GFP-f: 5'-TGAAGGTGATGCAACATACGG-3' (~~Seq. No. 4~~ SEQ ID NO:4)

GFP-r: 5'-GTCTTGTAGTTCCCGTCATC-3' (~~Seq. No. 5~~ SEQ ID NO:5)

Please replace the paragraph starting at page 13, line 3 with the following paragraph:

The peptide vector according to the present invention can transmit genes to all kinds of cells without tissue specific tropism, unlike conventional virus vectors-as well as, and does not induce host immune responses, due to its small size corresponding to ~~[[a]]~~ the level of a hapten.